Proposed for Early Diagnosis of Vulvovaginal Candidiasis Using Oncotic Cytology

Proposta de Protocolo para Diagnóstico Inicial de Candidíase Vulvovaginal a Partir de Citologia Oncótica
Protocolo Propuesto para el Diagnóstico Inicial de la Candidiasis Vulvovaginal Basado en la Citología Oncótica

RESUMO
Objetivo: Avaliar o desempenho da citologia oncótica na detecção de leveduras e propor um protocolo para o diagnóstico precoce da candidíase vulvovaginal. **Método:** Estudo observacional, transversal, realizado de agosto de 2021 a novembro de 2023, composto por 358 amostras cérvico-vaginal. Foram determinados os parâmetros de desempenho diagnóstico comparando a citologia oncótica com a cultura micológica, enquanto os sinais e sintomas clínicos foram considerados como referência diagnóstica. **Resultados:** Identificaram-se leveduras em 5% (18/358) dos esfregaços citológicos e em 15,6% (56/358) das culturas. A citologia oncótica apresentou especificidade e valor preditivo positivo de 100%, valor preditivo negativo de 88,8% e acurácia de 89,4%, evidenciando associação com o diagnóstico definitivo de candidíase vulvovaginal. **Conclusão:** A citologia oncótica constitui uma ferramenta inicial útil, embora não deva ser empregada isoladamente para excluir a infecção. O enfoque polifásico proposto pode otimizar o diagnóstico precoce, minimizar erros e promover uma atenção integral à saúde feminina.
DESCRITORES: Vulvovaginite; Teste de Papanicolaou; Levedura; Diagnóstico Precoce.

ABSTRACT
Objective: To evaluate the performance of cervical cytology in detecting yeast and propose a protocol for the early diagnosis of vulvovaginal candidiasis. **Method:** This was an observational, cross-sectional study conducted from August 2021 to November 2023, comprising 358 cervicovaginal samples. Diagnostic performance parameters were determined by comparing cervical cytology with mycological culture, while clinical signs and symptoms were considered as the diagnostic reference. **Results:** Yeast was identified in 5% (18/358) of cytological smears and in 15.6% (56/358) of cultures. Cervical cytology had a specificity and positive predictive value of 100%, a negative predictive value of 88.8%, and an accuracy of 89.4%, demonstrating an association with a definitive diagnosis of vulvovaginal candidiasis. **Conclusion:** Cervical cytology is a useful initial tool, although it should not be used alone to exclude infection. The proposed polyphasic approach can optimize early diagnosis, minimize errors, and promote comprehensive women's health care.
DESCRIPTORS: Vulvovaginitis; Papanicolaou test; Yeast; Early Diagnosis.

RESUMEN
Objetivo: Evaluar el desempeño de la citología oncótica en la detección de levaduras y proponer un protocolo para el diagnóstico precoz de la candidiasis vulvovaginal. Método: Estudio observacional y transversal realizado entre agosto de 2021 y noviembre de 2023, con 358 muestras cérvico-vaginales. Se determinaron los parámetros de rendimiento diagnóstico comparando la citología oncótica con el cultivo micológico, considerando los signos y síntomas clínicos como referencia diagnóstica. Resultados: Se identificaron levaduras en el 5% (18/358) de los frotis citológicos y en el 15,6% (56/358) de los cultivos. La citología oncótica presentó especificidad y valor predictivo positivo del 100%, valor predictivo negativo del 88,8% y exactitud del 89,4%, mostrando asociación con el diagnóstico definitivo de candidiasis vulvovaginal. Conclusión: La citología oncótica constituye una herramienta inicial útil, aunque no debe emplearse aisladamente. El enfoque polifásico propuesto puede optimizar el diagnóstico temprano y favorecer una atención integral a la salud femenina.
DESCRIPTORES: Vulvovaginitis; Prueba de Papanicolaou; Candidiasis; Diagnóstico precoz.

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INTRODUCTION

Vulvovaginal candidiasis (VVC) is a clinical condition caused by excessive yeast growth[1], resulting in signs/symptoms that can significantly affect a woman's quality of life. Its impact extends to emotional and social health, highlighting the importance of an approach in the context of women's health[2].

The prevalence of VVC varies according to regional factors, cultural habits, and health practices, and is a significant problem in gynecological services[3]. Furthermore, diagnosis of vulvovaginal candidiasis based solely on clinical data is questionable due to the similarity of signs and symptoms with other causes of vulvovaginitis[1]. Therefore, combining them with laboratory tests will contribute to a more accurate diagnosis and treatment[4].

The laboratory diagnosis of VVC is established based on mycological examination, including conventional culture and molecular biology[5]. However, these tests are expensive and are not readily available in the Brazilian Unified Health System (SUS). This is important in vulnerable communities, where lack of resources can lead to delayed diagnosis and inadequate treatment[6] .

In contrast, oncotic cytology, which involves the collection and analysis of cells from the cervix and vagina for the purpose of preventing and identifying neoplasms at an early stage, can reveal characteristics that suggest candidiasis at all stages of execution[7] .

In the medical history, it is possible to identify reports of intense vulvar pruritus, bleeding after sexual intercourse, and pain/burning when urinating, while in the inspection of the cervix/vagina, thick white vaginal discharge, fissures, hyperemia, and vulvovaginal edema are observed[8]. In cytological analysis, typical yeast morphology can be seen, such as pseudohyphae and/or budding, in addition to a higher number of leukocytes and cellular changes suggestive of inflammation[9].

Considering that the integration of cytology with clinical evaluation can contribute to the early identification of infection, the detection of candidiasis using the oncotic cytology test can lead to appropriate guidance and therapy, preventing recurrences and reducing the risk of complications. Immediate diagnosis of VVC can avoid more complex and expensive treatments in the future, as well as reduce the demand for emergency care, benefiting both patients and the healthcare system.

In this context, the present study aimed to evaluate the performance of oncotic cytology for the detection of yeast and propose a protocol for early detection of vulvovaginal candidiasis.

METHOD

This was an observational, cross-sectional study conducted from August 2021 to November 2023, comprising 358 cervicovaginal samples from women aged between 18 and 65 years in the Recôncavo region of Bahia. Women who sought public services for gynecological examinations and agreed to participate in the study by signing an informed consent form participated in the study. Women with no history of sexual activity and those who had undergone treatment for any urogenital tract pathology in the last 12 months were excluded.

Vaginal bleeding after sexual intercourse, itching and burning in the vaginal region, presence of thick white vaginal discharge (leucorrhea), and changes in the cervix/vagina,

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including edema, hyperemia, excoriations, fissures, and/or lesions, were evaluated based on the information recorded in the cytopathological examination request. Simultaneously, samples were collected for oncotic cytology and mycological culture.

A cytological smear was prepared using the conventional technique and subjected to Papanicolaou staining for yeast detection[2]. A swab of the cervicovaginal sample was seeded in Sabouraud Dextrose Agar supplemented with chloramphenicol and, after 48 hours at 35±1°C, positive cultures were subjected to Gram staining to confirm yeast[9].

Data were analyzed using GraphPad InStat version 3.05. Fisher's exact test, with a significance level of 5%, determined associations and calculated the parameters of sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of oncotic cytology, considering mycological culture as the gold standard. The diagnosis of candidiasis was defined by positive yeast culture and the presence of signs and/or symptoms.

Ethical approval was obtained from the Research Ethics Committee of the Maria Milza University Center, opinion No. 7,281,350, CAAE No. 36887120.6.0000.5025.

RESULTS

Yeast was observed in 5% (18/358) of cytological smears and in 15.6% (56/358) of mycological cultures. Considering oncotic cytology for the detection of yeast in comparison to mycological culture, the sensitivity of the test was 32.1% (95% CI 0.2026; 0.4593), the specificity was 100% (95% CI 0.9878;1.000), PPV of 100% (95% CI 0.8146;1.000), NPV of 88.8% (CI: 0.8496;0.9196), and accuracy of 89.4%.

Among the clinical signs and symptoms evaluated, only pruritus was associated with positive oncotic cytology for yeast, suggesting that women with this symptom may be 4.2 times more likely to have yeast in the oncotic cytology test (*RR* 4.207, 95% CI 1.716;10.314). Furthermore, it was possible to establish an association between the definitive diagnosis of candidiasis and oncotic cytology examination (Table 1).

Table 1: Association of signs/symptoms and diagnosis of vulvovaginal candidiasis with the presence of yeast observed in oncotic cytology tests. Recôncavo Baiano, Bahia, Brazil, 2021 to 2023.

	Yeasts present in oncotic cytology		p value*
	Present	Absent	
Signs and symptoms	18	340	0.051
Leucorrhea	8	120	0.291
Altered cervix/vagina	2	52	0.472
Bleeding after sexual intercourse	2	7	0.069
Itching	10	72	0.002
Burning	4	55	0.343
Vulvovaginal candidiasis			
Present	14	25	< 0.001*
Absent	4	315	

*Fisher's exact test

Based on the findings of this study, it was possible to propose a diagnostic protocol for vulvovaginal candidiasis based on oncotic cytology examination (Table 2).

able 2: Protocol for the initial diagnosis of vulvovaginal candidiasis based on oncotic cytology. Recôncavo Baiano, Bahia, Brazil, 2021 to 2023.

Objective
To establish guidelines for the use of oncotic cytology testing in the screening of yeast infections, defining procedures for positive, negative, and doubtful cases.
Diagnosis and Conduct
Stage 1: Collection and evaluation of oncotic cytology The test must be performed following the quality criteria for cervicovaginal cytology The report should indicate the presence or absence of yeast

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Step 2: Interpretation of Results and Conduct	
Oncotic cytology result for yeast	**Conduct**
Positive	Symptomatic, treat. Asymptomatic, assess need for treatment or monitoring only.
Negative and asymptomatic patient	No action required.
Negative and patient with suggestive symptoms	Suspected false negative. Proceed to additional tests
Step 3: Additional Tests in Suspected Cases	
Fungal culture	**Molecular test**
Sabouraud agar or chromogenic agar	Polymerase chain reaction
Identifies yeast species	High sensitivity
Detects antifungal resistance	Useful in samples with low fungal load
Long time to get results	Higher cost and less accessible
Step 4: Treatment Based on Results	
Result	**Conduct**
Confirmed infection - positive oncotic cytology or positive complementary test	Antifungal treatment according to clinical guidelines.
No evidence of infection - negative oncotic cytology + negative complementary examination	Reassess differential diagnosis - bacterial vaginosis, trichomoniasis, irritant dermatitis, allergies

DISCUSSION

Oncotic cytology, traditionally used in cervical cancer screening, can also play a complementary role in the detection of CVV. The observation of fungal structures in cytological smears represents a valuable diagnostic opportunity, especially in regions where access to specific mycological tests is still limited[10-12]. However, the observed diagnostic performance indicates that cytology, although highly specific, has limitations in terms of sensitivity, which requires careful interpretation of negative results.

The high specificity observed demonstrates that morphological identification of yeasts in cytological smears is a reliable finding with high confirmatory value, minimizing the occurrence of false-positive diagnoses. This characteristic gives oncotic cytology significant clinical relevance, since it allows healthcare professionals to safely institute antifungal treatment, provided there is a correlation between the laboratory findings and the symptoms presented by the patient. This perspective is in line with international studies that have highlighted oncotic cytology as a relevant auxiliary method in the diagnosis of VVC[13,14].

The test's ability to identify yeast in the form of blastoconidia or pseudohyphae, stained brownish-gray to eosinophilic[2,9], allows oncotic cytology testing to also play an important role in women's health through regular monitoring of CVV. Consequently, it enables the SUS to implement education and prevention programs, contributing to the reduction of the incidence of this condition, which affects about 75% of women in adulthood[15].

On the other hand, the limitation in analytical sensitivity reinforces that the absence of yeast in cytology does not completely rule out the possibility of infection, especially in cases of low fungal load or when there is a predominance of the non-budding form, which is more difficult to recognize under a microscope. The obscuring of fungal cells by epithelial cell overlap, cell debris, and leukocytes, as well as smear analysis at 40x magnification, standardized for cytological analysis, can also make it difficult to observe yeast on the stained slide[16].

The significant association between vulvar pruritus and cytological positivity observed in this study reinforces the role of this symptom as an important clinical marker of vulvovaginal candidiasis[17]. Itching, unlike other nonspecific genital symptoms, reflects the local inflammatory response mediated by yeast, especially in *Candida albicans* infections[18]. This clinical association strengthens the relevance of medical history and detailed physical examination in the interpretation of laboratory results, highlighting the need for an integrated approach between cytology and clinical practice. The absence of a significant association with other symptoms illustrates the difficulty in differentiating candidiasis from other vaginitis based solely on clinical manifestations, which justifies the importance of complementary methods of laboratory confirmation[1,19].

The association between oncotic cytology and the clinical-mycological diagnosis of CVV reinforces the potential of this test as an auxiliary tool in the screening of fungal infections. The presence of yeast on the cytological slide should be interpreted as a possible indication of active infection, especially in symptomatic patients. This perspective is in line with studies that advocate the use of routine cytopathological tests for the recognition of infectious agents, optimizing resources and strengthening women's health surveillance actions[10,14].

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The proposed protocol therefore emerges as a practical strategy to guide the diagnostic management of CVV in the context of public health services. By including interpretation steps based on clinical symptoms and positive cytology, the protocol favors more targeted approaches and avoids the indiscriminate use of antifungals. In addition, by providing for culture and molecular testing in suspected or recurrent cases, it proposes a stepped model that combines diagnostic efficiency and rationalization of laboratory resources, an essential principle in the primary care networks of the Brazilian Unified Health System[2,5].

From an epidemiological point of view, the inclusion of yeast testing in cytological examination represents an advance in the monitoring of fungal infections of the female genital tract, especially in regions where the prevalence of VVC may reflect specific environmental, socioeconomic, and behavioral factors. Strengthening oncotic cytology testing in the identification of this fungal infection can contribute to broader gynecological health surveillance and the development of local indicators of vulvovaginal infection, strengthening preventive actions.

Finally, in oncotic cytology, it is important to consider some methodological limitations that influence data interpretation, such as the quality of the sample collected and the observer's experience in identifying fungal structures, which can lead to diagnostic variability. In addition, the lack of identification of fungal species limits the understanding of the etiological profile of the infection, especially in view of the increased occurrence of *non-albicans* yeasts, often associated with antifungal resistance[15]. These factors reinforce the need to incorporate confirmatory methods whenever possible.

CONCLUSION

Oncotic cytology can be considered a useful and accessible tool in the initial approach to VVC, especially in primary care settings. Its integration into well-structured clinical-laboratory protocols can expand the diagnostic capacity of services and promote more effective care for women's health.

The proposed protocol represents a practical contribution to the incorporation of oncotic cytology testing into the screening of fungal infections in the context of primary health care. Thus, it is considered that the systematic use of oncotic cytology as an auxiliary tool in the screening of VVC can increase the effectiveness of health services, especially in regions with limited access to mycological tests.

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